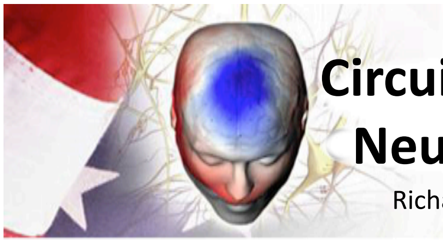


Circuit Simulation Approaches to Extending Neuronal System Simulation and Design.

Richard Schiek[1], Christina Warrender[2], Hongyou Fan[3] & Conrad James[4]
Sandia National Laboratories, Albuquerque, NM
[1]Electrical and Microsystems Modeling, [2]Cognitive Systems Research,
[3]Ceramic Processing and Inorganic Materials, [4]Advanced Sensor Technologies

Introduction

Simulation of neural systems opens many avenues of discovery. Through detailed, *neural-circuit* simulation, we are investigating:

- extraction of governing parameters from large experimental data sets
- understand the dynamics and stability of natural systems
- constraining the design of new, experimental systems.

Approach

- Circuit Simulation: Xyce

  To model a system of interacting neurons, we use Sandia's parallel, electrical circuit simulator, Xyce. Without any loss of generality, Xyce allows us to solve detailed, ordinary differential equation models for neuron membrane potentials, ion concentrations and channel currents as well as pre and post synapse dynamics. Because Xyce is a parallel code, the simulation of very large systems (i.e. over 10^6 neurons) is possible.

- Uncertainty Quantification: Dakota

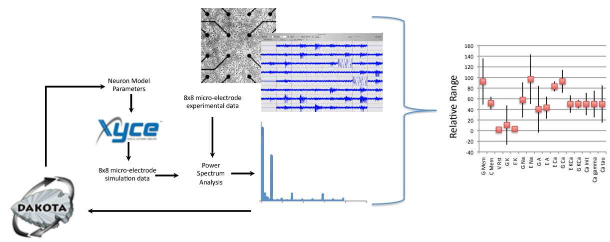
  However, direct simulation alone provides only part of the dynamical picture of how neuronal systems work. We employ Sandia's optimization and uncertainty quantification package, Dakota, to constrain and control the model parameters and topology of our neural systems.

  Using Xyce and Dakota together allows one to not only optimize the fit of a simulation to some standard, but also discover system stability and sensitivity of modeling parameters.

- Experimental Benefits

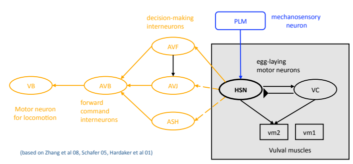
  Simulations designed to mimic experiments and extract modeling parameters or examine stability can illuminate the information content of an experiment. This analysis has been applied to *in vitro* cultures and soon will be applied to *in vivo* measurements with quantum dots.

Using Fourier analysis for parameter extraction



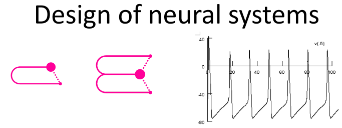
By coupling simulation with fitting to experimental data, we can find not only an optimal fit, but the range within which the simulations dynamically behave the same as the experiments.

Understanding the egg-laying motor circuit in *C. elegans*



- Common microcirciut motif
- Feed-forward excitation, feedback inhibition
- Understanding its functional properties may aid understanding of more complex systems that include this microcircuit
- From simulations we can find a set of conductance parameters which produce experimentally observed calcium oscillations.

Design of neural systems



- Aid the design of neural circuits with desired properties
- Start with simplest single-neuron circuit – autapse
- Calibration: measure and model spontaneous firing rate.
- How does cell morphology and circuit topology affect firing rate and signal transmission?

Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000.